REMARKS

This is a full and timely response to the non-final Office Action mailed by the U.S. Patent and Trademark Office on February 2, 2008. Claims 1-8, 11-18 and 21-23 remain pending in the present application. Claims 1, 6, 11, 16 and 21 are amended. No new matter is introduced. The specification is amended to correct minor typographical errors. In view of the foregoing amendments and following remarks, reconsideration and allowance of the present application and claims are respectfully requested.

Objections to the Specification

The Office Action states that the disclosure is objected to for a minor informality. Applicant has amended the specification to correct the typographical error mentioned in the Office Action, and to correct a number of other minor typographical errors.

Accordingly, Applicant respectfully requests that the objection to the specification be withdrawn.

Claim Objections

The Office Action objects to claims 1, 11 and 21. Regarding claim 1, the Office Action states that "[c]laim 1 does not provide punctuation after the limitation "population" in line 4 of the first obtaining step."

Applicant has reviewed claim 1 and finds a comma "," after the term "population" in claim 1, line 4.

Applicant has amended claims 1, 11 and 21 as suggested in the Office Action. Accordingly, Applicant respectfully requests that the objections to the claims be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-8, 11-18 and 21-23 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 1, 11 and 21

The Office Action states that the term "said region" in line 2 of the "analyzing" step

lacks antecedent basis. Applicant has amended claim 1 to provide antecedent basis for the term "said region" in line 2 of the "analyzing" step.

The Office Action states that claim 1 recites the limitation "members are selected from one or both of: people affected with a genetic disease or trait in said inbred population and parents of people affected with said genetic disease or trait in said inbred population" in lines 2-3 of the obtaining step. The Office Action then states that "[h]owever, the "analyzing" step only includes finding a region in genomes of the affected people or a region in genomes of parents of the affected people, in lines 1-2 of the "analyzing" step." Applicant has amended claim 1 to recite "analyzing the actual and estimated genotype data to find one or both of a region in genomes of the affected people and a region in genomes of parents of the affected people."

The Office Action states that "claim 1 in lines 3-4 of the "analyzing: step and claim 11 in lines 6-7, recite the limitation "markers exhibiting particular homozygous pairs of alleles more frequently than would occur randomly." The Office Action then states that "[t]he specification and claims do not provide a clear and precise definition of what encompasses "more frequently than would occur randomly."

Applicant directs the Examiner's attention to the specification, page 3, lines 1-8, which states:

> [t]he invention addresses this need through techniques of using statistical analysis of genetic data to determine likely regions in the genome based upon markers there for a recessive genetic disease or trait. One embodiment of these techniques includes the steps of obtaining actual genotype data for one or more affected people with the genetic disease or trait in a population and/or actual genotype data for their parents, obtaining estimated genotype data for the population, and analyzing the actual and estimated genotype data to find a region in the genome of the affected people that includes markers exhibiting particular homozygous pairs of alleles more frequently than would occur randomly.

Further, the specification, page 16, line 5 to page 17, line 3; and page 18, lines 7-11, further defines the terms "autozygous" and "not autozygous." Applicant respectfully submits that, after review of the specification, one skilled in the art would understand the term "more frequently than would occur randomly."

The Office Action states that "claim 1 in lines 1-3 of the "determining" step, claim 11 in lines 8-10 and claim 21 in lines 12-13, recite the limitation "determining a set of scores for

each of said markers in said actual and estimated genotype data relative to each person for which actual genotype data was determined." The Office Action then states that "[o]ne skilled in the art would be unclear as to how markers that are in actual and estimated genotype data, are then relative to each person for which actual genotype data was determined."

Applicant directs the Examiner's attention to the specification, page 15, lines 4-10, which describe the term "actual genotype data" by stating:

> [i]n step 31, actual genotype data is determined for one or more affected persons with the genetic disease under consideration. This genotype data is not a full sequencing of the person's DNA. Rather, the genotype data is an identification of particular alleles at a selected set of markers in the person's DNA. For example, a set of SNP markers could be determined for the affected person(s). Such genotyping is far less expensive than full DNA sequencing.

Applicant also directs the Examiner's attention to the specification, page 15, lines 12-22, which describe the term "estimates" by stating:

> [i]n step 32, estimates are obtained of genotype frequency data for the entire inbred population to which the affected persons and their parents belong. When determining these estimates, it can be assumed that the alleles a child gets for any marker from his or her parents are independent.
>
> In one embodiment, the estimates are found by actually genotyping a subset of the population. An error rate e for the estimates can be assumed, with the presence of the error indicating that a measured value in the genotyping is a result of a random selection from the population. Standard statistical techniques can be used to determine the error rate e from the size of the subset and the size of the overall population under consideration. Other techniques can be used to find the estimates without departing from the invention.

Applicant also directs the Examiner's attention to the specification, page 16, line 1 to page 17, line 16, which describes "determining scores" by stating:

> Scores are determined in step 33 for the markers selected for the genotyping. A score is determined in turn for each marker relative to each affected member or parent for which actual genotype data was determined in step 31.
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> FIG. 4 shows a table with probability calculations that can be used to determine the scores according to one embodiment of the invention. Several variables are used in these calculations, as follows:
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> n=a number of alleles possible for the marker under consideration,

designated as A, B, C, etc.--for markers that are SNPs, n is usually two;

p_X=the estimated frequency of allele X in the population, as determined in step 32, with X being one of A, B, C, etc. (e.g., p_A=the estimated frequency of allele A at the marker, p_B=the estimated frequency of allele B at the marker, etc.);

p_X^M=the probability that an affected person got allele X at the marker under consideration from his or her mother--if the mother's genotype at the marker is known, this can be determined using standard Mendelian genetics and will be 0, 0.5, or 1; otherwise p_X is used;

p_X^F=the probability that an affected person got allele X at the marker under consideration from his or her father--if the father's genotype at the marker is known, this can be determined using standard Mendelian genetics and will be 0, 0.5, or 1; otherwise p_X is used.

In order to find a score for a marker relative to an affected person or parent of an affected person, the row of the table in FIG. 4 is selected that corresponds to the observed genotype data for that person or parent. The calculations in that row are performed to determine probabilities of observing that marker given various types of autozygosity with the founder and also the probability of observing that marker in the absence of autozygosity.

For each marker, this process is repeated relative to each affected person or parent of an affected person for whom actual genotype data is available. The result is a collection of scores for each marker representing probabilities of different types of autozygosity relative to each affected person or parent, as illustrated in FIG. 5.

Markers will receive higher scores for some forms of homozygosity as compared to other forms. The forms that receive the higher scores tend to be more likely to be associated with the genetic disease or trait.

The tables in FIG. 4 and FIG. 5 can be expanded using basic rules of symmetry to accommodate other possible combinations of alleles. These tables can also be expanded to more complex pedigree information (i.e., grandparents).

Applicant respectfully submits that, after review of the specification, one skilled in the art would understand the terms "actual" and "estimated" "genotype data" and would understand the feature "determining a set of scores for each of said markers in said actual and estimated genotype data relative to each person for which actual genotype data was determined," as recited in claims 1, 11 and 21.

The Office Action states that "claim 1 in line 4 of the "determining" step, claim 11 in line 11 and claim 21 in lines 14-15, recite the limitation "probabilities of observing each marker given autozygosity with a founder." The Office Action then states that "[o]ne skilled in the art would be unclear as to whether the person with the marker is autozygous with a founder or what the marker relationship to autozygous pertains or what is meant by given

autozygosity with a founder."

Applicant directs the Examiner's attention to the specification, page 16, line 22 to page 17, line 16, which describe the term "autozygosity with a founder" by stating:

> In order to find a score for a marker relative to an affected person or parent of an affected person, the row of the table in FIG. 4 is selected that corresponds to the observed genotype data for that person or parent. The calculations in that row are performed to determine probabilities of observing that marker given various types of autozygosity with the founder and also the probability of observing that marker in the absence of autozygosity.
>
> For each marker, this process is repeated relative to each affected person or parent of an affected person for whom actual genotype data is available. The result is a collection of scores for each marker representing probabilities of different types of autozygosity relative to each affected person or parent, as illustrated in FIG. 5.
>
> Markers will receive higher scores for some forms of homozygosity as compared to other forms. The forms that receive the higher scores tend to be more likely to be associated with the genetic disease or trait.
>
> The tables in FIG. 4 and FIG. 5 can be expanded using basic rules of symmetry to accommodate other possible combinations of alleles. These tables can also be expanded to more complex pedigree information (i.e., grandparents).

Applicant respectfully submits that, after review of the specification, one skilled in the art would understand the feature of "probabilities of observing each marker given autozygosity with a founder," as recited in claims 1, 11 and 21.

The Office Action states that "claim 1 in lines 5-6 of the "determining" step, claim 11 in lines 12-13 and claim 21 in lines 15-16, recite the limitation "probabilities of observing each marker given absence of autozygosity with a founder." The Office Action then states that "[o]ne skilled in the art would be unclear as to whether the person with the marker is autozygous with a founder or what the marker relationship to autozygous pertains or what is meant by given absence of autozygosity with a founder."

Applicant directs the Examiner's attention to the specification, page 16, line 22 to page 17, line 16, which describe the term "absence of autozygosity with a founder" by stating:

> In order to find a score for a marker relative to an affected person or parent of an affected person, the row of the table in FIG. 4 is selected that corresponds to the observed genotype data for that person or parent. The calculations in that row are performed to determine probabilities of observing that marker given various types of autozygosity with the founder and also the

probability of observing that marker in the absence of autozygosity.

For each marker, this process is repeated relative to each affected person or parent of an affected person for whom actual genotype data is available. The result is a collection of scores for each marker representing probabilities of different types of autozygosity relative to each affected person or parent, as illustrated in FIG. 5.

Markers will receive higher scores for some forms of homozygosity as compared to other forms. The forms that receive the higher scores tend to be more likely to be associated with the genetic disease or trait.

The tables in FIG. 4 and FIG. 5 can be expanded using basic rules of symmetry to accommodate other possible combinations of alleles. These tables can also be expanded to more complex pedigree information (i.e., grandparents).

Applicant respectfully submits that, after review of the specification, one skilled in the art would understand the feature of "probabilities of observing each marker given absence of autozygosity with a founder," as recited in claims 1, 11 and 21.

The Office Action states that "claim 1 in line 25, claim 11 in line 18 and claim 21 in line 20, recite the limitation "whether said marker is not autozygous." The Office Action then states that "[o]ne skilled in the are would not understand how a marker, defined as a genetic sequence in the specification, page 7, line 18, can be or not be autozygous. An organism carrying two alleles and can be autozygous but it is unclear how a single sequence can be autozygous."

Applicant directs the Examiner's attention to the specification, page 17, line 18 to page 18, line 11, which describes whether a marker is "not autozygous" by stating:

Next, in step 34, the scores are merged.

First, scores for each type of autozygosity for each marker are multiplied together. For example, in FIG. 5, scores in group 41 are multiplied together, scores in group 42 are multiplied together, and scores in group 43 are multiplied together. This is repeated for all markers.

Second, the products for each type of autozygosity are summed weighted by the probability of that allele for that marker in the population. For example, the products from multiplying groups 41, 42 and 43 are summed. This is repeated for all markers. The result is a score representing the likelihood of observing the actual measured value for the marker given that the marker is autozygous (i.e., homozygous and inherited from the founder).

Third, scores for the "not autozygous" case for each marker are multiplied together. For example, scores in group 44 are multiplied together. This is repeated for all markers. The result is a score representing the likelihood of observing the actual measured value for the marker given that

the marker is not autozygous and comes independently from the overall population distribution (i.e., is not from the founder).

Applicant respectfully submits that, after review of the specification, one skilled in the art would understand the feature of "whether said marker is not autozygous," as recited in claims 1, 11 and 21.

Claims 6 and 16

Applicant has amended claims 6 and 16 to recite "merged scores."

Accordingly, Applicant respectfully submits that claims 1-8, 11-18 and 21-23 are in compliance with 35 U.S.C. § 112, second paragraph, and respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. § 101

Claims 1-8, 11-18 and 21-23 stand rejected under 35 U.S.C. § 101, as allegedly being directed to non-statutory subject matter. The Office Action states that "[t]he claims are drawn to a method of using statistical analysis of genetic data from an inbred population to determine likely genetic regions for a recessive genetic disease or trait," and then states "there is no physical transformation by the claimed invention, thus the Examiner must determine if the instant claims produce a useful, tangible, and concrete final result." The Office Action then states that "claims 1-8, 11-18, 22 and 23 do not produce a tangible final result," and further states that "because the method claims are draw to nonstatutory subject matter for not producing a useful, concrete and tangible result, the system that performs the process also does not produce a useful concrete and tangible result, thus also drawn to nonstatutory subject matter."

Applicant has amended claims 1 and 11 to recite "sequencing DNA in said at least one contiguous region to identify the recessive allele associated with said genetic disease or trait." Applicant has amended claim 21 to recite "(g) sequencing DNA in said one or more contiguous regions of markers to identify the recessive allele associated with said genetic disease or trait." Support for this feature can be found in the specification, at least on page 21, lines 8-15. This feature provides a useful, concrete and tangible result.

Accordingly, Applicant respectfully submits that claims 1-8, 11-18 and 21-23 are in compliance with 35 U.S.C. § 101, and respectfully request that the rejection be withdrawn.

CONCLUSION

For at least the foregoing reasons, Applicant respectfully requests that all outstanding rejections be withdrawn and that all pending claims of this application be allowed to issue. If the Examiner has any comments regarding Applicant's response or intends to dispose of this matter in a manner other than a notice of allowance, Applicant requests that the Examiner telephone Applicant's undersigned attorney.

Respectfully submitted,

SMITH FROHWEIN TEMPEL GREENLEE BLAHA LLC
Customer No. 35856

By: /Michael J. Tempel/
Michael J. Tempel
Registration No. 41,344
(770) 709-0056